

## **REMARKS/ARGUMENTS**

Claims 119-123 remain pending in this application. Applicants respectfully traverse the present rejections.

### **Claim Rejections – 35 U.S.C. §101**

Claims 119-123 stand rejected under 35 U.S.C. §101 because, allegedly, “the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.” (Page 2 of the instant Final Office Action).

The Examiner maintains that “the instant application, as filed, fails to provide any evidence that the instant PRO830 polypeptides are specifically associated with lung cancer.” (Page 4 of the instant Final Office Action). The Examiner has relied on the teaching of Anderson *et al.* to show that allegedly, strong opposing evidence exists on the topic of predicting protein expression from corresponding mRNA levels. Applicants have discussed the references by Anderson *et al.* in great detail in their Response dated December 7, 2006 and maintain their position regarding this matter.

Further, Applicants would like to bring to the Examiner’s attention a recent decision by the Board of Patent Appeals and Interferences (Decision on Appeal No. 2006-1469). In its decision, the Board reversed the utility rejection, acknowledging that “there is a strong correlation between mRNA levels and protein expression.” Applicants submit that, in the instant application, the Examiner has likewise not presented any evidence specific to the PRO830 polypeptide to refute Applicants’ assertion of a correlation between mRNA levels and protein expression. Accordingly, Applicants respectfully request that the outstanding rejections be withdrawn and this case passed to issue.

The Examiner further alleges that “Applicants’ Response is absolutely silent with respect to the main argument presented by the Examiner, which is the total lack of explanation presented in the instant specification as why one skilled in the art would consider a DNA, which is slightly amplified....to be useful as a marker for lung cancer.” (Page 3 of the instant Final Office Action). Applicants first respectfully point out that the observed increase in PRO830 gene amplification in lung tumor is **significant**, as has been discussed in detail in the previous responses. Applicants have repeatedly argued that gene amplification, an essential mechanism

for oncogene activation, is well-described in Example 170, page 539 onwards of the present application. Gene amplification was monitored using real-time quantitative TaqMan™ PCR and the results are set forth in Table 9B. As explained in the passage on page 539, lines 37-39, "the results of TaqMan™ PCR are reported in  $\Delta$ Ct units. **One unit** corresponds to one PCR cycle or approximately a **2-fold amplification**, relative to control, two units correspond to 4-fold, 3 units to 8-fold amplification and so on." (Emphasis added). Applicants show that PRO830 showed **2.188 to 2.549-fold** amplification in lung tumors, which is significant and thus the PRO830 gene has utility as a diagnostic marker of human lung cancer.

Applicants maintain that the specification, as filed, provides sufficient disclosure to establish a specific, substantial and credible utility for the PRO830 polypeptide of SEQ ID NO:175 and that the increase in gene amplification for the DNA encoding PRO830 is sufficient to confer patentable utility to the instantly claimed PRO830 polypeptides. Example 170 explicitly states that the PRO830 DNA is significantly overexpressed in lung tumors as compared to the normal control.

As discussed previously, it is not a legal requirement to establish a "necessary" correlation between an increase in gene copy number and protein expression levels or to find evidence that protein levels can be accurately predicted from gene amplification data. Instead, as discussed before, the evidentiary standard to be used throughout *ex parte* examination of a patent application is a preponderance of the totality of the evidence under consideration. Accordingly, the question is rather if it is more likely than not that a person of ordinary skill in the pertinent art would recognize such a positive correlation between gene amplification levels and protein levels. Applicants respectfully submit that when the proper evidentiary standard is applied, a correlation must be acknowledged.

Applicants maintain that, both Polakis Declarations (Polakis I and II) and the teachings in the art, represented by the 149 references presented in the IDS of August 17, 2006, support Applicants' assertion, in general, that changes in mRNA level generally lead to corresponding changes in the level of the expressed protein. Applicants submit that considering the evidence as a whole, with the overwhelming majority of the evidence supporting Applicants' asserted utility, a person of skill in the art would conclude that Applicants' asserted utility is "more likely than not true." *Id.*

Therefore, Applicants request that the Examiner reconsider this rejection and maintain that they have demonstrated utility for the PRO830 polypeptide and the antibodies that bind to it. Applicants add that the gene amplification data clearly supports a role for PRO830 as a lung tumor marker. Accordingly, the present 35 U.S.C. §101 utility rejections should be withdrawn.

**Claim Rejections – 35 U.S.C. §112, First Paragraph**

Claims 119-123 stand further rejected under 35 U.S.C. §112, first paragraph, since allegedly “the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, one skilled in the art clearly would not know how to use the claimed invention.”

For the reasons outlined above, Applicants maintain that one skilled in the art would know how to make and use the instant invention (PRO830 antibodies), based on the disclosures in the specification and the knowledge in the art, and use it as a lung tumor marker. Accordingly, the present rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

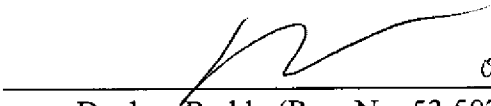
Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney’s Docket No. **39780-2730 P1C10**).

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: July 12, 2007

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